

SECOND SUPPLEMENTAL PRELIMINARY AMENDMENT  
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Claim 5. (Twice Amended) The isolated nucleotide molecule according to claim 4, wherein said nucleotide molecule comprises the nucleotide sequence shown in Figure 2 (SEQ ID NO:1).

Claim 6. (Amended) The isolated nucleotide molecule according to claim 1, wherein said lgs gene product is human Legless (hLgs) protein.

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Claim 7. (Twice Amended) The isolated nucleotide molecule according to claim 6, wherein said nucleotide molecule comprises the nucleotide sequence shown in Figure 10A (SEQ ID NO:16).

Claim 8. (Twice Amended) An isolated nucleotide molecule having at least 50% homology to (a) the nucleotide sequences shown in Figure 2 (SEQ ID NO:1) and Figure 10A (SEQ ID NO:16) or (b) complements or fragments thereof.

Claim 9. (Amended) The isolated nucleotide molecule according to claim 8, wherein said fragments are probes for use in hybridization assays.

Claim 10. (Amended) A vector comprising the nucleotide molecule according to claim 1.

Claim 11. (Amended) The vector of claim 10, wherein said nucleotide molecule is operably linked to control sequences recognized by a host cell transformed with said vector.

Claim 12. (Amended) A host cell comprising the vector of claim 10, wherein said host cell is selected from the group consisting of mammalian, bacterial, yeast, plant and insect cells.

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Claim 13. (Amended) An isolated polypeptide encoded by the nucleotide molecule of claim 1, derivatives, fragments and analogs thereof.

Claim 14. (Amended) The polypeptide of claim 13, wherein said polypeptide comprises Legless proteins.

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Claim 15. (Amended) An isolated polypeptide sharing one or more homologue amino acid domains with a Legless protein and being a functional homologue of a Legless protein.

Claim 16. (Amended) The polypeptide according to claim 15, wherein said functional homologue is the hLgs/Bcl-9 protein or a fragment thereof, and has the function of a Legless protein in the Wnt-pathway.

Claim 17. (Amended) A method for isolating a Lgs-binding protein comprising co-immunoprecipitating a Lgs-binding protein in a sample using the polypeptide of claim 13.

Claim 18. (Amended) A process for producing a polypeptide comprising culturing a host cell comprising the vector of claim 10, under conditions suitable for expression of said polypeptide and recovering said polypeptide or fragment thereof from the cell culture, wherein said host cell is selected from the group consisting of mammalian, bacterial, yeast, plant and insect cells.

Claim 19. (Amended) An antibody which specifically binds to the polypeptide of claim 13, wherein said antibody is selected from the group consisting of polyclonal antibodies, monoclonal antibodies, humanized antibodies and single chain antibodies.

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cont } Claim 20. (Amended) A chimeric molecule comprising the polypeptide of claim 13 or a fragment thereof fused to a heterologous amino acid sequence.

Claim 21. (Amended) The chimeric molecule according to claim 20, wherein said heterologous amino acid sequence is selected from the group consisting of an epitope tag sequence, a glutathione-S-transferase moiety, a thioredoxin moiety, and an antibody moiety.

Claim 23. (Amended) An isolated peptide, comprising at least one sequence homology domain which is common between *Drosophila* Legless proteins and human Legless proteins.

Claim 24. (Amended) The peptide according to claim 23, wherein the human Legless proteins are hLgs-1 or hLgs/Bcl9.

C3 Claim 25. (Amended) A compound which interferes with the binding of partner proteins to the at least one sequence homology domain according to claim 23.

Claim 26. (Amended) The compound according to claim 25, wherein said partner proteins are selected from the group consisting of Doll and  $\beta$ -Catenin.

Claim 27. (Amended) The compound according to claim 26, wherein said compound is selected from the group consisting of small peptides, synthetic polymers, and natural or synthetic chemical compounds.

Claim 28. (Amended) The compound according to claim 27, wherein said compound is a small peptide comprising the sequence homology domain 1 of figure 7B (SEQ ID NOs:2-3) or the sequence homology domain 2 of figure 7B (SEQ ID NOs:4-5).

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Claim 29. (Amended) A pharmaceutical composition for delivering said small peptide of claim 28 or a vector encoding the same, into a cancerous cell comprising said small peptide or vector; and a pharmaceutically acceptable carrier.

Claim 30. (Amended) A synthetic molecule, wherein said molecule simulates the function of Legless proteins in the Wnt pathway.

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cont } Claim 31. (Amended) An antagonist of the polypeptide of claim 13, wherein said antagonist is selected from the group consisting of small bioorganic molecules, synthetic polymers, and small polypeptides.

Claim 32. (Amended) An agonist of the polypeptide according to claim 13, wherein said agonist is selected from the group consisting of small polypeptides, and small bioorganic molecules.

Claim 33. (Amended) A method of screening for agonists and/or antagonists of the polypeptide claimed in claim 13 comprising screening a chemical library for compounds which inhibit the interaction of Lgless proteins and a partner protein using a reagent that detects said interaction.

Claim 35. (Amended) An isolated antisense oligonucleotide which hybridizes to the nucleotide molecule according to claim 1.

C4 } Claim 36. (Amended) The antisense oligonucleotide according to claim 35, wherein said oligonucleotide hybridizes to RNA and/or genomic DNA encoding a vertebrate Lgs.

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Claim 37. (Amended) The antisense oligonucleotide according to claim 36, wherein said oligonucleotide prevents translation of said RNA or transcription of said DNA.

Claim 38. (Amended) The antisense oligonucleotide according to claim 35, wherein said oligonucleotide comprises chemically modified nucleotides or nucleotide analogs.

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Claim 39. (Amended) A method of treatment of diseases caused by over-activation of the Wg pathway comprising administering, to a subject in need of such treatment, a pharmaceutically effective amount of the antisense oligonucleotide of claim 35.

Claim 40. (Amended) An isolated double-stranded RNA molecule corresponding to the nucleotide molecule according to claim 1, wherein said RNA molecule has RNA interfering activity.

Claim 41. (Amended) The double-stranded RNA molecule according to claim 40, wherein said double-stranded RNA molecule is effective to induce degradation of lgs single-stranded RNA.

Claim 42. (Amended) A method for reducing lgs gene expression in an invertebrate or vertebrate organism or an invertebrate or vertebrate cell line comprising contacting said organism or cell line with an amount of said double stranded DNA molecule of claim 40 sufficient to reduce lgs gene expression therein.

Claim 43. (Amended) A pharmaceutical composition comprising an oligonucleotide derived from the nucleotide molecule according to claim 1, and a pharmaceutically acceptable carrier, wherein said oligonucleotide and said carrier are passable through a cell membrane.

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Claim 44. (Amended) A pharmaceutical composition comprising the polypeptide of claim 16, and a pharmaceutically acceptable carrier, wherein said polypeptide and said carrier are passable through a cell membrane.

Claim 45. (Amended) The pharmaceutical composition according to claim 43, wherein said oligonucleotide is effective to reduce expression of a mammalian Lgs protein.

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cont } Claim 46. (Amended) The pharmaceutical composition according to claim 43, wherein said oligonucleotide is coupled to a moiety that inactivates mRNA.

Claim 47. (Amended) The pharmaceutical composition according to claim 46, wherein the moiety that inactivates mRNA is a ribozyme.

Claim 48. (Amended) The pharmaceutical composition according to claim 43, wherein the pharmaceutically acceptable carrier comprises a structure which binds to a receptor on a cell surface, wherein said structure is taken up by the cell after binding to said receptor.

Claim 49. (Amended) The pharmaceutical composition according to claim 43, wherein said oligonucleotide is a double stranded RNA molecule derived from the nucleotide molecule according to claim 1, wherein said RNA molecule possesses RNA interfering activity.

Claim 50. (Amended) The pharmaceutical composition according to claim 49, wherein the double stranded RNA molecule comprises 18 to 1000 nucleotides.

Claim 51. (Amended) A method for treatment of cell fate disorders comprising administering, to a subject in need of such

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treatment, a pharmaceutically effective amount of a compound selected from the group consisting of Lgs proteins, homologues thereof, functional homologues, and nucleotide molecules encoding the same and/or fragments thereof.

Claim 52. (Amended) The method according to claim 51, wherein said cell fate disorders are disorders in cell differentiation or proliferation.

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Claim 53. (Amended) The method according to claim 51, wherein said compound is selected from the group consisting of invertebrate and vertebrate Lgs protein homologues or fragments thereof, antibodies, antibody fragments, Lgs antisense DNA, lgs antisense RNA, lgs double-stranded RNA, small peptides, and chemical or natural compounds which interfere with Lgs function, synthesis and degradation.

Claim 54. (Amended) The method according to claim 51, wherein the compound is administered to treat a cancerous condition.

Claim 55. (Amended) The method according to claim 51, wherein the compound is administered to prevent progression from a pre-neoplastic or non-malignant condition to a neoplastic or malignant state.

Claim 56. (Amended) The method according to claim 51, wherein the compound is administered to treat a cancerous condition characterized by over-stimulation of the Wnt pathway.

Claim 57. (Amended) The method according to claim 56, wherein the cancerous condition is selected from the group consisting of colon, breast, head and neck, brain, thyroid, medulloblastoma and skin cancer.

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Claim 58. (Amended) The method according to claim 51, wherein the compound is administered to treat a blood disease.

Claim 59. (Amended) The method according to claim 51, wherein the compound is administered to promote tissue regeneration and repair.

Please add the following new claims:

-- Claim 61. A method for isolating a Lgs-binding proteins comprising co-immunoprecipitating a Lgs-binding protein in a sample using the polypeptide of claim 14.

Claim 62. An antibody which specifically binds to the polypeptide of claim 14, wherein said antibody is selected from the group consisting of polyclonal antibodies, monoclonal antibodies, humanized antibodies and single chain antibodies.

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Claim 63. A chimeric molecule comprising the polypeptide of claim 14 or a fragment thereof fused to a heterologous amino acid sequence.

Claim 64. An antagonist of the polypeptide of claim 14, wherein said antagonist is selected from the group consisting of small bioorganic molecules, synthetic polymers, and small polypeptides.

Claim 65. An agonist of the polypeptide according to claim 14, wherein said agonist is selected from the group comprising small polypeptides, and small bioorganic molecules.

Claim 66. The pharmaceutical composition according to claim 50, wherein the double stranded RNA molecule comprises 20 to 500 nucleotides.



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Claim 67. The pharmaceutical composition according to claim 66, wherein the double stranded RNA molecule comprises 20 to 50 nucleotides.

Claim 68. The pharmaceutical composition according to claim 67, wherein the double stranded RNA molecule comprises 20 to 22 nucleotides.

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Claim 69. A method for isolating a Lgs-binding protein comprising assaying for binding of a test protein to the chimeric molecule of Claim 20, and isolating a test protein which binds in said assay so as to isolate said Lgs-binding protein, wherein said assay is selected from the group consisting of an *in vitro* binding assay, a co-immunoprecipitation assay using a vertebrate or invertebrate cell lyzate and a mammalian or yeast two hybrid binding assay.

Claim 70. A method for diagnosing cell fate disorders comprising assaying for the presence of anti-Lgs antibodies, Lgs proteins or homologues thereof, lgs nucleic acids and/or fragments thereof in a test sample from a subject, wherein said assay is selected from the group consisting of a GST-fusion protein *in vitro* binding assay, a co-immunoprecipitation assay and a yeast two hybrid binding assay. --

REMARKS

Claims 1, 4-21 and 23-59 have been amended to place them in proper form in accordance with U.S. Patent practice. Further support for the amendments to Claim 1 can be found in cancelled Claims 2-3. Claims 22 and 60 have been cancelled and new